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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/017,472	CHADA ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7-23,25,32-43,69-73 and 75-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 7-23, 25, 32-43, 69-73, 75-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment, declaration, and response filed 2/28/07 are acknowledged. Claims 3, 74 have been canceled. Claims 1, 4, 36, 69, 78 have been amended. Claims 1, 2, 4, 7-23, 25, 32-43, 69-73, 75-78 are pending and under current examination.

The reply filed on 6/15/06 does not comply with the Revised Amendment Practice of 37 CFR 1.121 (See OG Notice 23 September 2003). Specifically, claim 2 is generic and under examination, and thus should not be identified as "withdrawn". Appropriate correction is required.

Election/Restrictions

The claims under examination are subject to an election of invention and species requirement, see the office action mailed on 2/24/03. In the response received from the applicant dated 3/17/03 and 7/7/03, the applicant elected without traverse of group I, drawn to a method of using a mda-7 nucleic acid(s), and the species drawn to treating an angiogenesis-dependent cancer, using the fragment 182-206 of SEQ ID No: 2, and adenoviral vector for examination on the merits. Applicant later filed a petition requesting rejoin of non-elected invention, which was granted-in-part. Applicant now amended claims so that Claims 3, 4, 77, and 78 are limited to the elected species (angiogenesis-dependent cancer) concerning the genus of angiogenesis related diseases. It is noted in view of the decision on petition, the full length and various fragments of the mda-7 have been included in the examination (claims 25, 32, 68-74). It

is also noted claims 36 and 37 have now been amended to read on the elected invention, using a nucleic acid for treatment. Claims 1, 18-23, 38, however, are generic and have not been amended to reflect the elected subject matter. All pending claims, including generic claims 1, 2, 7-24, 33-43, 75-77, have been examined **only** to the extent that they read on treating angiogenesis-dependent cancer using a nucleic acid expressing human MDA-7.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 2/26/07 cited unpublished U.S. patent applications, which are not suitable to be listed on the face of the patent, and thus they have been considered but lined through from IDS.

The references C150 and C151 do not comply with the requirement of 37 CFR 1.97. because they do not list the publication date. If the applicant intends to resubmit the references, please only resubmit the references that have been lined through.

It is also noted reference C19 submitted 5/2/2002 does not list the publication date, appropriate correction is required.

Specification

The amendment to Specification filed on February 2007 appears to be an intent to change inventorship. However, such can only be done through procedures outlined in 37 CFR 1.48.

Accordingly, the amendment has not been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 7-23, 25, 32-43, 69-73, 75-78 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *intratumoral* injection of a nucleic acid expressing a full length MDA-7 polypeptide or secreted form of MDA-7 (lacking a secretion signal, i.e. the fragment 49-206 of SEQ ID No: 2) for treating angiogenesis-dependent cancer, does not reasonably provide enablement for distal or systemic administration of an adenoviral vector expressing any *fragment* of MDA-7 polypeptides for treating angiogenesis-dependent tumor, for reasons of record.

Unless otherwise noted, the arguments in the instant response that have been addressed in the previous Office actions will not be reiterated, but will be referred to a previous Office action.

a. Systemic vector delivery for cancer gene therapy.

Pertaining to the arguments of *Miller et al*, and *Makrides et al*, please see page 10 of the Office action mailed 6/15/2004. Further, Applicant argues *Miller et al* is drawn to treating a different disease, not cancer. However, gene delivery is an universal issue in gene therapy no matter what disease is being treated, i.e. whether the treatment is for cancer or for cystic fibrosis, one needs to address how to deliver sufficient therapeutic

agent to significant numbers of target cells as taught by *Miller et al*; and it is necessary to select an efficient vector delivery system as taught by *Makrides et al.*

As to the support of therapeutic effect *in vivo* and the declaration of Dr. Chada, please see page 11 of the Office action mailed 6/15/2004, where the Office noted that the art of record and Dr. Chada only provides enablement for intratumoral injection (see § 9 of the Declaration).

Applicant then cited a post-filing publication WO 04/078124, where the authors implanted encapsulated 293 cells expressing sMDA-7 in the upper right flank, and the growth of tumor xenografts in the lower right flank was suppressed. Applicant argues that this proves that systemic administration is feasible.

In response, it is noted the aforementioned approach is drawn to a different invention, because it does not administering a nucleic acid systemically as instantly claimed, wherein a nucleic acid reaches target cells from a remote injection site. The aforementioned approach implanted a device (encapsulated 293 cells genetically modified) where MDA-7 is secreted and released to the circulation, which simulates the effect of administering a MDA polypeptide rather than administering a nucleic acid containing MDA-7 gene systemically, and thus the working example of the cited post-filing art can not be used to support the instantly claimed invention.

Moreover, the instant disclosure fails to teach implanting encapsulated and transfected 293 cells for *in vivo* MDA-7 delivery. In the instant specification, transfectant 293 cells were used for *in vitro* viral replication and for producing purified MDA-7 *in vitro*. The court has stated (*In re Glass*, 181 USPQ 31, (CCPA 1974)), IF A DISCLOSURE IS

INSUFFICIENT AS OF THE TIME IT IS FILED, IT CANNOT BE MADE SUFFICIENT, WHILE THE APPLICATION IS STILL PENDING BY LATER PUBLICATIONS WHICH ADD TO THE KNOWLEDGE OF THE ART SO THAT THE DISCLOSURE, SUPPLEMENTED BY SUCH PUBLICATIONS, WOULD SUFFICE TO ENABLE THE PRACTICE OF THE INVENTION. INSTEAD, SUFFICIENCY MUST BE JUDGED AS OF THE FILING DATE; SECTION 132 PROHIBITS ADDING NEW MATTER TO DISCLOSURE AFTER FILING". in *In re Glass*, the appellant attempted to use the disclosures of four patents issued after his filing date, and court ruled, "IF INFORMATION TO BE FOUND ONLY IN SUBSEQUENT PUBLICATIONS IS NEEDED FOR SUCH ENABLEMENT, IT CANNOT BE SAID THAT THE DISCOSURE IN THE APPLICATION EVIDENCES A COMPLETED INVENTION... IT IS AN APPLICANT'S OBLIGATION TO SUPPLY ENABLING DISCLOSURE WITHOUT RELIANCE ON WHAT OTHERS MAY PUBLISH AFTER HE HAS FILED AN APPLICATION ON WHAT IS SUPPOSED TO BE A COMPLETED INVENTION", "IF HE CANNOT SUPPLY ENABLING INFORMATION, HE IS NOT YET IN A POSITION TO FILE.

b. Targeted viral vector delivery.

With respect to arguments concerning viral vectors, applicant is referred to pages 7-8 of the Office action mailed 9/20/03, and the section bridging pages 13-14 of the Office action mailed 6/15/04.

With respect to arguments concerning adenoviral vectors, as an initial matter, the instant claims are drawn to any viral vector not limited to adenoviral vector. Further, applicant points to numerous art of record arguing that adenoviral vector can infect various cell types and tissues.

In response, this very feature of adenoviruses is actually a showing for why targeted gene delivery is necessary: because systemic adenoviral vector delivery would result in dissemination of adenovirus to various tissues and organs, rather than targeted

to the desired tissue/cells, and would lead to more vector allotment in tissues having adenoviral tropism. Besides, the host immune response against adenoviral vector has been a well-known barrier for systemic use of adenovirus in gene therapy because of unwanted immune response and fast elimination of the vector from the host (e.g. *Nasz et al*, Acta Microbiol Immunol Hung 2001;48:323-48). Accordingly, for reasons of record and set forth *supra*, the rejection stands.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 75 and 76 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and following.

Claims 75 and 76 recite the limitation "viral particles". There is insufficient antecedent basis for this limitation in the claim.

In the remarks, Applicants insists that the skilled artisan would understand that the number of viral particles recited in claims 75 and 76 refer to the amount of viral vector [of claim 8] that is administered to a patient.

In response, a viral vector may encompass a viral particle, the concept "viral particle" and "viral vector" is not equivalent to the skilled artisan in biology, and from the perspective of English language. The specification fails to redefine the two phases as being equal alternatives.

Further, claim 9 depends from claim 8 and is directed to administer the viral vector at 10^3-10^{13}, while claim 75, also depends from claim 8 and recites administering viral particles at 10^{10} to 10^{11}. It is unclear whether the substance administered in the two claims are the same or different, and whether or how the dosing regimen for claim 9 and claim 75 comparable. Thus the metes and bounds of the claims are uncertain.

It is applicant's responsibility to clarify the matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 7-23, 25, 35-43, 69-73, 75-78 stand provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/615,154 which has a common inventor with the instant application, for reasons of record.

Claims 1, 2, 4, 7-23, 25, 35-43, 68-73, 75-77 stand rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. U.S. patent application 09/615,154 has a different inventive entity, yet the disclosure anticipates the instantly claimed invention, for reasons of record and following.

The declaration under 37 CFR 1.132 filed 2/28/07 is insufficient to overcome the rejection of claims based upon 102(f) as set forth in the previous Office action because: the name of the inventor Elizabeth Grimm is missing.

Claim Rejections - 35 USC § 102/103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 7, 8, 10-15, 25, 32-36, 42, 43, 69-73, 77, and 78 stand rejected under 35 U.S.C. 102(e) as being anticipated by or in the alternative under 35 U.S.C. 103(a) as obvious over *Fisher* (US 6,355,622), and as evidenced by *Folkman et al* (Nature 1989;339:58-61; and J Biol Chem 1992;267:10931-4), for reasons of record and following.

Fisher teaches a method of inhibiting cancer in a subject comprising intratumoral administering, to nude mice bearing human cervical carcinoma cells, replication deficient adenoviral vector encoding the full length mda-7 protein (e.g. column 6, lines 27-65), wherein the full length mda-7 is a polypeptide comprises amino acid 1-206 of SEQ ID No: 2, and various fragments as recited in claims 32, 69-74; wherein the administration regimen was three times a week for 4 weeks. *Fisher* reports the growth of well-established tumors were inhibited in the mda-7 treated mice compared to the

control group (column 14, lines 35-67), wherein the expression of mda-7 was driven by a CMV promoter (column 13, line 56). *Fisher* also teaches that the nucleic acid could be embedded in liposome and introduced into cells (column 3, line 67, lipid composition). *Fisher* also tested anti-cancer effects of mda-7 on other human cancer cell types, which include nasopharyngeal carcinoma (head cancer, column 5, line 67), and glioblastoma (neuroblastoma, column 6, line 6). *Fisher* teaches that ectopic expression of mda-7 inhibits the growth of tumor cells and may provide therapeutic benefit for the treatment of human cancer (column 14, lines 62-65). Although *Fisher* did not directly administer the nucleic acid encoding MDA-7 in a human patient, they did test the MDA-7 effect on *human* cancer cells in nude mice (e.g. table 1, column 14, and figure 5). Thus, *Fisher* clearly teaches a method for treating tumor in a human patient. Given the correlation and success in the *in vitro* and *in vivo* study on human cancer cells as taught by *Fisher*, one would have had a reasonable expectation of success using such method in human patients. Thus the claimed invention was at least *prima facie* obvious over, if not anticipated by *Fisher*.

It is noted that *Fisher* does not literaterally teach that tumor is an angiogenesis-related disease. However, it was well known in the art that tumor belongs to angiogenesis-related disease, and angiogenesis accompanies tumor growth and metastasis as evidenced by *Folkman et al*, which has been cited in the previous Office action thus the teaching of *Fisher* meets every claim limitation for the elected species.

Therefore, *Fisher* anticipates, or in the alternative, renders the instant claims obvious.

Response to Arguments

In the Remark, the applicant again argued that *Fisher* does not even mention angiogenesis or inhibition of angiogenesis, accordingly, it does not anticipate the claimed invention.

The argument has been addressed in pages 7-11 of the previous Office action mailed 1/10/2006, and will not be reiterated.

The applicant then argued just because a tumor is an angiogenesis-disease does not mean that every agent that treats tumors is going to inhibit angiogenesis. Applicant also cited Fisher discussion concerning the mechanism of mda-7 action, and concluded again that Fisher does not teach suppressing tumor via inhibit angiogenesis.

The argument has been fully considered but found not persuasive for reasons of record and following:

The invention as claimed fully encompasses the method taught by *Fisher* in the aspect of anti-cancer effect of the mda-7, and in the aspect of method steps. Even though that *Fisher* does not teach that the MDA-7 anti-tumor effect was, at least in part, through suppressing angiogenesis, it was known that adenovirus expressing mda-7 is capable of inhibiting tumor growth whatever the mechanism might be. In fact, *Fisher* did suggest that the knowledge at the time could not explain how mda-7 functions to suppress various cancers, and suggests, as cited by the applicant, "THE INHIBITION IN CANCER GROWTH INDUCED BY MDA-7 CAN OCCUR BY MULTIPLE PATHWAYS" (see page 16 of the Remark). The court has decided it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. In re

Woodruff, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); In re Swinehart, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and Ex Parte Novitski, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Accordingly, the rejection stands.

Further, the specification fails to teach the tumor treated by *Fisher* is not angiogenesis-dependent, and thus, as long as Fisher's method suppressed tumor growth, it intrinsically also suppressed tumor angiogenesis. The specification fails to teach suppressing tumor growth does not necessarily suppress tumor angiogenesis; and the specification fails to teach that tumor growth is independent of angiogenesis, and it appears *Fisher* meets *every* element of instantly claimed invention

Applicant then argues *Fisher* did not intrinsically teach inhibiting angiogenesis in a human patient because the treatment was effected in mice, not humans.

In response, it is noted *Fisher* conducted the *in vitro* and *in vivo* studies on various types of human cancer cells, even though the human cells were implanted into a mouse for the *in vivo* study for obvious reasons. *Fisher* differs from instant disclosure in that they did not actually administering the nucleic acid into a human subject. But given the results of *Fisher* study, there are no obvious reasons on record why intratumoral injection of the same nucleic acid expressing MDA-7 would not suppress the same type of tumor and tumor angiogenesis in a human subject.

Applicant then argues that the results in the present specification were surprising and unexpected because in the prior art, a role for MDA-7 was provided solely in the context of terminal differentiation and apoptosis, not angiogenesis.

In response, applicant is reminded that the combined the teachings have established that it was known in the art that MDA-7 suppress cancer cell growth, even though the applicant claiming to have revealed an underlying mechanism that may be unknown in the art at the time. Applicant is reminded, it is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff*, 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed.Cir. 1990); *In re Swinehart*, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993).

Applicant also argues not all cancers are angiogenesis-dependent cancers, and submitted several publications supporting the arguments.

In response, again, the elected invention is drawn to angiogenesis-dependent cancer, and the applicant fails to establish that the cancer taught by Fisher were not angiogenesis-dependent.

Accordingly, for reasons of record and set forth *supra*, the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7-9, 16-23, 36-41, 75, 76 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Fisher* (US 6,355,622), in view of *Roth et al* (US 6,069,134), and as evidenced by *Nasz et al* (Acta Microbiol Immunol Hung 2001;48(3-4):323-48).

As discussed in the immediate preceding section, *Fisher* teaches intratumoral injection of adenovirus encoding MDA-7 for treatment of cancer, and administering the vector to tumor cells *in vitro* at moi of 10^2pfu/cell, but does not specify the dosage for *in vivo* administration (column 14, line 22). *Fisher* teaches that ectopic expression of mda-7 inhibit the growth of tumor cells and may provide therapeutic benefit for the treatment of human cancer in general, but did not discuss the details of such therapy (column 14, lines 62-65), nor the combined cancer treatment regimen.

Roth et al supplemented *Fisher* by establishing that these limitations were routine in the art for treating cancer in humans. *Roth et al* detailed a method comprising administering a DNA damaging agent (e.g. cisplatin) combined with adenoviral vector expressing a tumor suppressor (e.g. p53, abstract), together with conventional chemotherapy and surgery for the treatment of cancer (column 3, lines 20-48). *Roth et al* teach that the DNA damaging agents include gamma-irradiation, x-rays and UV-irradiation, for example; and the chemotherapeutic agents include 5-fluorouracil (column 4, lines 57-67). *Roth et al* teach that local administration was preferred method, but intravenous infusion from a site distal of tumor was contemplated (column 30, lines 40-64). *Roth et al* also teach that the adenoviral stock was administered at a m.o.i. of 10^8 pfu/ml (column 12, line 1). Moreover, *Roth et al* further evidences that the *in vitro* and mice studies of a candidate agent on human cancer cells are feasibility studies for

treating a human patient, and applying such method in humans is a logical extension of the experimental studies.

Claims 20-23 and 37-41 are limitations for the timing of the combination therapy, neither *Roth et al nor Fisher* discuss the details. However, given the levels of the ordinary skilled in the art, these limitations would fall within the bounds of the optimization for a proper therapeutic regimen.

Claims 75 and 76 are drawn to the total dose of viral vectors applied to an individual ranging from 10^{10} to 10^{13}. Although *Fisher* in view of *Roth* does not teach the particular doses, it was well known in the art replication defective adenoviral vectors can be produced in very high titers (e.g. *Nasz et al*, abstract), and it was clearly within the levels of the skill to figure out a proper amount of viral vectors needed for achieving therapeutic effects.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method as taught by *Fisher* in treating a human subject using the regimens as taught by *Roth et al* by administering the mda-7 either prior or after the conventional therapy at a dosage sufficient for tumor cell killing with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the combined therapy would maximize the tumor-treating effect by any individual therapy alone. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

The applicant first argued that claim limitations are not taught by the combination of references because neither *Roth* nor *Fisher* mentions angiogenesis.

In response, as discussed on record, instant claims clearly acknowledge a method of inhibiting angiogenesis encompasses treating cancer (say text of instant claims 1-4). Clearly, cancer is a species of the genus of angiogenesis related diseases, which has been clearly taught by *Fisher et al* (e.g. column 5, lines 32-43) in view of *Roth et al* (e.g. abstract, column 3, lines 20-48). This is because it is well established that a species of a claimed invention renders the genus obvious. In re Schaumann, 572 F.2d 312, 197 USPQ 5 (CCPA 1978).

Applicants then argue that claimed invention was surprising and unexpected, which argument has been addressed in the section *supra*, and will not be reiterated.

Applicants then argue that there is no reasonable expectation of success as neither reference discusses angiogenesis, the skilled artisan would not have any reason to believe that combining the teachings of the references would provide a way to inhibit angiogenesis in a patient.

In response, the instant claims clearly indicated that the recited angiogenesis encompasses cancer angiogenesis, which is the elected species for the type of diseases, and it is well known in the art that tumors are angiogenesis dependent. Since both references teach the method suppressed tumor growth, one would have had a reasonable expectation of success combining the two methods for treating cancer, an angiogenesis-associated disease. Accordingly, since *Fisher et al* taught the success of

inhibiting tumor with a nucleic acid expressing MDA-7, and since *Roth et al* taught the success in combining conventional therapy with gene therapy in treating tumor, a skilled artisan would have had a reasonable success in inhibiting the tumor, an angiogenesis associated disease, when combined the gene therapy with the conventional cancer therapy. Accordingly, the rejection stands.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 4, 7-24, 25, 32, 35-43, 69-73, 77, 78 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 92-116,125-154, 159-174 of copending U.S. Patent Application No. 09/615,154, for reasons of record and set forth *supra*, particularly considering all of the limitations of cited claim 173 are taught in the instant disclosure and the cited application. Applicant is reminded that the elected species for the disease treated is angiogenesis-dependent **cancer**, and Claim 173 reads (emphasis added),

173. (Currently amended) A method for **treating a patient with cancer** comprising
1) administering to the patient by intratumoral injection an effective amount of an expression construct **comprising a nucleic acid sequence encoding a full-length human MDA-7 polypeptide** or
a.[secreted] human MDA-7 polypeptide lacking the first 48 amino acids of SEQ ID NO:2 under the control era promoter operable in eukaryotic cells and
2) providing to the patient at least one other anticancer therapy, wherein the other anticancer therapy comprises a) performing surgery; b) administering chemotherapy; c) administering radiotherapy; or d) administering immunotherapy, wherein the cancer is non-small cell lung, small-cell lung, lung, hepatocarcinoma, retinoblastoma, astrocytoma, gum, tongue, neuroblastoma, head, neck, pancreatic, renal, testicular, ovarian, mesothelioma, cervical, gastrointestinal, lymphoma, brain, colon, or bladder.

In view of such, the reasoning for this rejection is self-explanatory. As to the second element of claim 173, it is encompassed by instant claims as evidenced by claims 1 and 21-23.

Claims of this application substantially conflict with claims 18, 70-74 of Application No. 10.378,590; and claims 38-41 of Application No. 11/156,521 because the claims in the cited application clearly or implicitly read on treating cancer in a human patient with a nucleic acid encoding mda-7. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on 571-272-0739. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

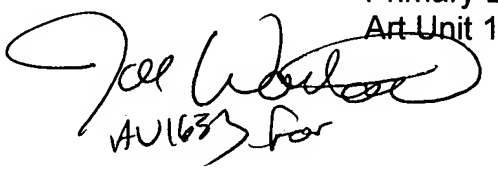
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633



QJL
June 7, 2007